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Validation of a therapy-oriented complication grading system in carotid endarterectomy surgery

MASTERARBEIT

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Abstract

Background and Purpose: The Clavien-Dindo- Grade (CDG) is a therapy-oriented grading system that classifies complications in response to necessary therapy in five grades (CDG 1= lowest grade, CDG 5= highest grade). The aim of this study is to validate CDG in a defined neurosurgical patient population with extracranial carotid artery stenosis who underwent carotid endarterectomy (CEA).

Methods: Patients were retrieved from a prospectively-collected database of patients who underwent CEA at the Department of Neurosurgery, University Hospital Zurich between January 2015 and March 2018. Complications at discharge and short-term follow-up (3 months after surgery) were rated by CDG. Patients' outcomes and neurological status were graded with the modified Rankin Scale (mRS) and National Institute of Health Stroke Scale (NIHSS).

Results: 119 patients underwent surgeries for a total of 120 CEAs (one patient received both-side CEA). 108 patients received treatment for symptomatic carotid artery stenosis. At discharge, ten (8.4%) patients showed some deviation from the normal post-operative course (CDG ≥ 1), with a median CDG of 2. Three (2.5%) of these complications were additionally graded with a "d" indicating new neurological deficits. None of the patients treated for asymptomatic carotid artery stenosis (n=11) presented any deviation from the normal post-operative course (CDG ≥ 1). Patients with higher CDG had significantly higher NIHSS ($p=0.001$; $R_2 =1$) and significantly higher mRS ($p= 0.001$; $R_2 =1$). The complication group was associated with a longer stay in hospital ($p<0.0001$).

Conclusion: Our study has demonstrated the correlation between clinically-relevant outcome scales (mRS and NIHSS) and the length of hospital stay with CDG in a well-defined neurosurgical patient population. These results show that CDG is a valid instrument for classifying early complications after CEA.

1. List of abbreviations

CAS Carotid artery stenting
CCI Comprehensive complication index
CDG Clavien-Dindo-Grade
CEA Carotid endarterectomy
CTA Computed tomography angiography
DUS Duplex ultrasound
ICA Internal carotid artery
KISIM Klinikinformationssystem
MCA Middle cerebral artery
MR Magnetic resonance
MRA Magnetic resonance angiography
mRS Modified Rankin Scale
NASCET North American Symptomatic Carotid Endarterectomy Trial
NIHSS National Institute of Health Stroke Scale
TIA Transient ischemic attack

2. Introduction

Carotid endarterectomy (CEA) is an effective surgical procedure to reduce the risk of ischemic stroke in patients with high-grade extracranial carotid artery stenosis.[1]

2.1. Definitions and etiology

Ischemic stroke is the second most common cause of death in Europe and the most common reason for acquired disability.[2] Ischemic stroke is defined as a focal, occasionally global, loss of neurological function over 24 hours with underlying vascular etiology. Similar events lasting under 24 hours are called a transient ischemic attack (TIA).

The main cause of carotid disease is a result of atherosclerosis with the deposition of cholesterol and fibrotic tissue in the arterial wall due to genetic and lifestyle factors. In Caucasians, it is mostly found in the extracranial carotid bifurcation.[2]

Extracranial atherosclerotic disease accounts for up to 15-20% of all ischemic strokes.[3,4] A clear correlation between the degree of stenosis and the risk of stroke was documented in the North American Symptomatic Carotid Endarterectomy Trial (NASCET).[5]

2.2. Measurement of stenosis severity

Conventional digital subtraction angiography (DSA) is the gold standard for evaluating the true severity of internal carotid artery stenosis.

However, non-invasive tests – carotid duplex ultrasound (DUS), magnetic resonance angiography (MRA), and computed tomographic angiography (CTA) – are preferred in current clinical practice because DSA is an invasive procedure associated with a possible risk of stroke and other complications.[6]

NASCET criteria uses the normal distal ICA as a denominator and are based on DSA. Nowadays, the degree of stenosis is rather estimated measuring velocity of the flow with DUS. Categorization is made into mild (0-49%), moderate (50-69%) and severe (70-99%) stenosis.[7]

2.3. Prevention

Medical advances in recent years along with aggressive cardiovascular risk factor modifications have resulted in reduced recurrence rates of atherosclerotic stroke. Recent medical breakthroughs in the primary and secondary prevention of atherosclerotic stroke through lifestyle modifications and novel treatment of modifiable risk factors for atherosclerosis play a crucial role in the treatment of affected patients.[8] Primary prevention is made by avoiding the development of a carotid disease through lifestyle modification, as recommended by the American Heart Association (AHA) guidelines.[9]

Secondary prevention focuses on reducing the clinical impact in patients with asymptomatic diseases. 10-15% first-ever stroke patients have had a previously-

untreated asymptomatic carotid artery stenosis.[7] Moderate stenosis in asymptomatic patients over 65 years can be found in about 2% of the population.[7]

Tertiary prevention is made to reduce recurrent stroke due to carotid stenosis in symptomatic patients. A carotid artery stenosis is defined as symptomatic if symptoms presented within the preceding 6 months. Symptoms might be hemi-sensory impairment, hemi-motor deficits and higher cortical dysfunction, mostly appearing as a loss of function.

Risk factors for plaque progression are smoking, high blood pressure, obesity, male sex and age over 65 years.[7]

Therapy

The goal of primary and secondary prevention is to reduce the risk factors through adapting one's lifestyle. Medical prevention in both types is achieved with lipid-lowering medication, management of hypertension with blood pressure goals <140/90mmHg and strict glycemic control in diabetic patients.[7]

Antiplatelet therapy with aspirin (75 or 325 mg daily) is recommended for patients with obstructive or non-obstructive atherosclerosis for preventing ischemic events, although the benefit has not been established for preventing stroke in asymptomatic patients. In patients with extracranial carotid disease who have sustained ischemic stroke or TIA, antiplatelet therapy alone or the combination with dipyridamole is recommended.[7,10] The guidelines recommend that patients with >50% stenosis without intervention should be treated with ASS or Clopidogrel as part of the best medical therapy. Early Clopidogrel and ASS before CEA in symptomatic patients with >70% stenosis seem to reduce recurrent events. [7]

Tertiary prevention represents the treatment (surgical or endovascular) of symptomatic high-grade extracranial carotid stenosis. CEA is established as safe and effective by randomized controlled trials for reducing the risk of ischemic stroke in both symptomatic and asymptomatic patients with carotid artery atherosclerosis. Carotid artery stenting (CAS) is proposed as an alternative to CEA in selected cases.[10]

2.4. CEA

CEA comprises 1) exposing the carotid artery through a small neck incision, and 2) opening the carotid artery and removing the atherosclerotic plaque from the vessel wall. The goal of such a procedure is stroke prevention. It is a durable procedure but not a cure: although rare, the accumulation of atherosclerotic material can occur again.[7]

Indication and timing in symptomatic patients

CEA is recommended in patients reporting carotid territory symptoms within the preceding 6 months and who have a 70-99% carotid stenosis, provided that the documented procedural death/stroke rate is <6% (Class I – Level A). CEA should be considered in patients reporting carotid territory symptoms within the preceding 6 months and who have a 50-69% carotid stenosis, provided that the documented procedural death/stroke rate is <6% (Class IIa – Level A).[7] In patients with <50%

stenosis CEA can be considered if symptoms are recurring despite the best medical therapy.[7]

The maximum benefit is seen if CEA is performed within 14 days after the onset of symptoms.[11] Urgent CEA is defined as surgery within 48 hours of the clinical onset of symptoms: it is rarely performed and should be considered in situations such as crescendo TIAs or stroke in progress, or fluctuating thrombus.
It is recommended that most patients who have suffered carotid territory symptoms within the preceding 6 months, are aged >70 years and have 50-99% stenosis should be treated by CEA rather than CAS (Class I – Level A).

Indication in asymptomatic patients

In “average surgical risk” patients with an asymptomatic 60-99% stenosis, CEA should be considered in the presence of one or more imaging characteristics that may be associated with an increased risk of late ipsilateral stroke, provided that the documented perioperative stroke/death rates are <3% and the patient’s life expectancy exceeds 5 years (class IIA - Level B). Imaging/clinical criteria that might confer an increased risk of stroke on best medical treatment include silent infarction on neuroimaging, stenosis progression, large plaque area, ultrasound plaque characteristics such as plaque echolucency, intra-plaque hemorrhage on MRI, impaired cerebrovascular reserve, spontaneous embolization on trans-cranial Doppler ultrasound, and a history of contralateral TIA.[7]

High-risk patients for CEA

Anatomical or clinical factors significantly increasing the risk of complications after CEA are significant cardiac or pulmonary disease, contralateral laryngeal-nerve palsy, previous radical neck surgery, cervical radiation therapy, and recurrent stenosis after CEA.[7]

In these high-risk patients for CEA, CAS should be evaluated. If CAS is considered risky, best medical therapy alone with lifestyle adaptation should be considered as an option. [7]

Complications after CEA

Complications occurring immediately after CEA include intraoperative stroke with persisting neurological deficit and/or post-operative stroke. Furthermore, hemodynamic instability such as hypotension or more often hypertension can be seen.[12] Cranial nerve injuries such as recurrent laryngeal, hypoglossal or facial nerve palsy might appear immediately, although very few persist after one month.[2]

New post-operative ischemic lesions following CEA show an incidence between 8.8% and 12.2%.[2,13]

Classification of complications

In order to improve patients’ outcome, it holds importance to report and analyze surgery-related complications completely and objectively, mostly in a prospective fashion. The Clavien-Dindo-Grade (CDG) is a therapy-oriented grading system developed to classify surgical complications depending on the type of treatment required for a given complication. CDG rates any deviation from the normal and

expected post-surgical course in five grades. CDG was initially developed for visceral surgery.[14] Thereafter, it also proved to be a useful tool to rate complications in other surgical specialties, such as orthopedics, urology, gynecology,[15-17] and neurosurgery.[18,19]

CDG grade can either remain stable or worsen (increase) over time: in fact, any new complication occurring during the post-operative course will be considered and then graded. Therefore, CDG cannot improve (decrease) over time. This is in contrast to the outcome scales, which can both improve and worsen over time, depending on patients' clinical condition.

2.5. Study objective

The aim of this study is to test the applicability of CDG in a well-defined neurosurgical patient population who underwent CEA for carotid artery stenosis.

3. Methods

A retrospective study was performed using a prospectively-collected database of a well-defined cohort.

3.1. Setting and patients selection

Patients were retrieved from a prospectively-collected database of subjects who received CEA at the Neurosurgical Department of University Hospital between January 2015 and March 2018. The indication and type of treatment (CEA vs. CAS) of patients with carotid stenosis is discussed at the weekly multidisciplinary cerebrovascular board. All patients underwent a preoperative DUS examination as well as CTA and/or MRA.

Post-operative follow-up protocol includes routine clinical and radiological (by means of MRA or CTA) examination prior to discharge, as well as a short-term follow-up at 3 months after surgery including DUS.

3.2. Evaluation of the patient outcome

National Institute of Health Stroke Scale (NIHSS)

NIHSS quantifies neurological deficits after stroke (Table 2). The NIHSS comprises eleven items, each of which scores a specific ability between 0 and 4. A score of 0 indicates normal function in that specific ability, while a higher score is indicative of some level of impairment. The individual scores from each item are summed to calculate a patient's total NIHSS score. The maximum possible score is 42, while the minimum score is 0.[20]

Modified Rankin Scale (mRS)

mRS is a disability scale that is applied to measure the grade of disability after a stroke. The scale runs from 0 (no symptoms) to 6 (death). The modified Rankin Scale (mRS) is the most widely-used outcome measure in stroke clinical trials (Table 3).[21]

3.3. Complications graded by Clavien-Dindo grading system

CDG is a complication scale that registers any deviation of the normal post-operative course and classifies these deviations (complications) in five grades (from grade 1 to grade 5) based on the therapeutic consequences (Table 4, Figure 1).[3,4] CDG grade 1 contains any deviation from the normal post-operative course without the need for any intervention. CDG grade 2 complications require pharmacological treatment and CDG grade 3 complications require an intervention: for an intervention without general anesthesia, the complications is registered with CDG grade 3a and for intervention under general anesthesia with CDG grade 3b. CDG grade 4 registers patients with a life-threatening complication and need for an ICU stay (the complication is registered with CDG grade 4a if a single-organ dysfunction is present and CDG grade 4b in case of multi-organ dysfunction). The death of patients within 30 days is graded with CDG 5.[3,4] Moreover, in this study we introduce “d” as an additional marker for new

neurological deficits after CEA.

3.4. Statistical analysis

All statistical analysis were performed with GraphPad Prism 8 (https://www.graphpad.com/). T-tests, Fisher's exact test and Chi-square with Yates' correction were used for hypothesis testing. Significance was accepted at a p-value <0.05. The association between CDG and performance (mRS, NIHSS) or length of hospital stay was assessed using Spearman's rank correlation and presented with rho effect sizes and p-values. Rho was interpreted as follows: $0.0 \leq rho \leq 0.2$ shows no to very slight correlation, $0.2 \leq rho \leq 0.5$ shows slight to moderate correlation, $0.5 \leq rho \leq 0.8$ shows clear correlation and $0.8 \leq rho \leq 1.0$ shows high up to perfect correlation.

3.5. Ethics

Patient data and outcomes were prospectively collected in an institutional patient registry, which was approved upfront by the local ethics review board (Kantonale Ethikkommission PB-2017-00093) and internationally registered at clinicaltrials.gov (NCT01628406). Patient consent was waived due to the observational nature of the study. The scientific workup was approved upfront by the local ethics review board (Kantonale Ethikkommission KEK-ZH 2012-0244).

This master thesis was written using the STROBE Statement checklist for cohort studies.

4. Results

119 patients underwent a total of 120 CEAs (one patient received both-side CEA). 108 patients received treatment for symptomatic carotid artery disease.

4.1. Complications at discharge

At discharge, ten (8.4%) patients showed some deviation of the normal post-operative course (CDG ≥ 1), with a median CDG 2 (min. CDG 1 and max. CDG 5).

Three (2.5%) of these complications were additionally graded with a “d” indicating new neurological deficits. None of the patients treated for asymptomatic carotid artery diseases (n=11) presented any deviation of the normal post-operative course.

Patients with higher CDG had significantly higher NIHSS (p=0,001, R_2 =1) and significant higher mRS (p= 0,001, R_2 =1) at discharge.

By categorizing the patient population into a non-complication group (CDG 0) and a complication group (CDG ≥ 1), NIHSS significantly increased in the complication group (0(1) vs. 23(42), p< 0.0001) as well as mRS (1(1) vs. 5(6), p<0.0001).

4.2. Impact of complications on hospital stay

Patients stayed in hospital for 6.0 ± 4.2 days on average. The median stay in hospital was 5 days (range: 0 - 23 days). Any deviation from the normal post-operative course (CDG ≥ 1) was associated with a longer stay in hospital (11.9 ± 5.3 days vs. 5.7 ± 3.9 days, p-value < 0.0001). No statistical difference was seen in the length of hospital stay between patients with new neurological deficits (“d”) and those without “d” (10 ± 2.7 days vs. 12.7 ± 6.1 days; p= 0.49).

4.3. Complications at short-term follow-up (3 months)

At short-term follow-up (3 months), no new deviation of the normal post-operative course (CDG ≥ 1) was recorded.

5. Discussion

With the prospective use of the CDG system, we analyzed the well-defined patient population with carotid artery stenosis who underwent CEA. We showed a clear, statistically significant correlation between CDG and outcome grading systems (NIHSS and mRS) at discharge. Moreover, a significant correlation between CDG and patients' hospital stay was seen.

This study promotes CDG as an applicable grading system for complications after CEA.

5.1. Complications rates and comparison to literature

In our cohort, any deviation from normal post-operative course (CDG ≥1) at discharge was recorded in ten patients (8.3%), with a median of CDG 2. Three (2.5%) of these complications were additionally graded with a "d", thus indicating new neurological deficits.

Reported reasons of re-admission by others lie at 6.5% and comprise hemorrhage, vascular or graft complications, neurologic deficits, venous thromboembolism as well as perioperative complications such as cardiac, respiratory, urologic, renal, infectious and gastrointestinal incidents.[7]

In our cohort, one patient (0.8%) presented at discharge with persistent but asymptomatic stenosis. No symptomatic re-occlusion was registered at discharge and no symptomatic re-stenosis or re-occlusion was seen at short-term follow-up. DUS showed one (0.8%) new asymptomatic mild (10-40%) re-stenosis at 3 months follow-up. Brott[10] reported an overall rate of hemodynamically-significant re-stenosis in 5-7% after one year of follow-up.

The risk for cranial nerve injuries is 8.6%, according to NASCET.[22] In our cohort, two patients (1.7%) suffered from cranial nerve injury at discharge. At short-term follow-up, one of the patients had completely recovered, whereas the other had clearly improved.

In our cohort, one (0.8%) symptomatic stroke was seen at discharge. Literature reports an overall stroke rate of 7%.[22] One patient died, which expresses a mortality rate of 0.8% in our cohort. In literature[23], the overall death rate within 30 days was 3.1%.

5.2. Advantages and disadvantages of CDG

CDG provides a simple, reproducible, objective, and applicable therapy-oriented way of classifying post-surgical complications, which was precisely the aim of Clavien et al.[14] There is no subjective component, such as "minor" or "major" complications, and the grading system enables a comparison between case series in different institutions. The CDG score has been widely used in other surgical disciplines such as visceral or orthopedic surgery[15,16,24] and thus it facilitates comparisons between surgical specialties.[18] Furthermore, there is no underreporting of complications due to the registration of any deviation from the normal post-surgical procedure as a definition of the CDG grading system.

Several studies have shown that CDG is clinically relevant and associated with patients' outcome and the length of hospital stay in spine, orthopedic, and visceral surgery.[16,18,25-27] Nevertheless, it is not obvious that CDG can be used for cranial surgery where complications can cause severe neurological deficits. Some of the neurological complications do not demand sophisticated invasive treatments and are therefore graded low in CDG, although they may be associated with worse patient outcomes. The same concern was discussed by Bellut et al.[18] for patients undergoing lumbar spine surgery.

In the CDG classification of 2009,[14] the suffix "d" – which can be added to any CDG class – was used to indicate a persistent (disabling) complication at the time of discharge or follow-up that compromises health condition and is directly related to the treatment. Based on our experience with the use of CDG in neurosurgery,[28 18,19] we use the suffix "d" to indicate a new neurologic deficit after a neurosurgical procedure that is present at the time of discharge or follow-up.

5.3. Modifications of CDG grading system

Landriel-Ibañez et al.[29] developed a modified CDG score for cranial and spine procedures. As in CDG, the categories used to grade complications are based on the therapy used to treat the complications but labeled as follows: I (mild), II (moderate), III (severe), and IV (death). This score was presented as a simple and easily reproducible way to report negative outcomes based on the therapy administered to treat a complication.[29]
Schiavolin et al.[30] used the same Landriel-Ibañez classification system in 1,008 patients who underwent elective neurosurgical procedures. 14.3% of the patients had cerebrovascular diseases (e.g. aneurysm, cavernous hemangioma, arteriovenous malformations, and ischemic cerebral disease requiring bypass procedure). No subdivision of complications into the respective cerebrovascular disease group was performed; therefore, no comparison with our CEA cohort is possible. However, strong correlation with the Karnofsky performance scale was found.

5.4. Limitations

We arbitrarily decided to limit the follow-up analysis and CDG validation to 3 months. For patients who undergo CEA, this is the standard interval for post-operative routine visits, according to our protocol. Moreover, other published complication studies in neurosurgery also limited the follow-up time period similar to the one that we used.[18,29] Second, all analyses were carried out on data from a single reference center. Therefore, the study population is small due to a very selected cohort of patients who underwent CEA. Thus, we cannot generalize our results to other populations and centers with different decision protocols. We did not perform sub-group analysis or multivariate analysis for patients at high medical risk, which could have an impact on the incidence of complications due to the small study group. An external validation or major, multicenter study is required to confirm our findings.

5.5. Conclusion

CDG is an applicable grading system for classifying complications after CEA. A significant correlation between the CDG system and outcome scales (mRS and NIHSS) as well as between CDG and the length of hospital stay was documented. Moreover, in this study “d” was introduced as an additional marker for new neurological deficits (after CEA).

6. Literature

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7. Tables and Figures

Table 1 Baseline characteristics of our cohort

Male (%) / Female (%)	77 (65%) / 42(35%)
Mean age (range)	73 (45-95)
Cardiovascular risk factors: • Diabetes mellitus • Arterial hypertension • Smoking	 35 (29%) 93 (78%) 69 (58%)
Mean (±standard deviation) hospital stay	6.0 ± 4.2 days
Median hospital stay	5 days (range: 0 - 23 days)

Table 2. National Institute of Health Stroke Scale (NIHSS); (http://www.sw.org/misc/physicianresources/pdf/Neurology/neuro_nihstrokescale.pdf)

1a. **Level of Consciousness(LOC)** Arousal Status	Alert (or awakens easily and stays awake) Drowsy (Responds to minor stim. but falls back asleep) Obtunded (Responds only to deep pain or vigorous stim) Comatose (No response)	0 1 2 3
1b. **LOC**- Questions Month? Age?	Both questions answered correctly One question answered correctly Neither question answered correctly	0 1 2
1c. **LOC–** Commands Opens/closes eyes Opens/closes hands	Both commands performed correctly One command performed correctly Neither command performed correctly	0 1 2
2. **Eye Movements:** Horizontal eye movements	Normal Mild gaze paralysis (can bring eyes only over to midline) Complete gaze paralysis (deviated & unable to bring eyes over)	0 1 2
3. **Visual fields:** Sees objects in Four quadrants	Normal Partial hemianopia (upper OR lower quadrant) Complete hemianopia (upper AND lower quadrants) Bilateral hemianopia (total blindness)	0 1 2 3
4. **Facial:** Facial movements	Normal Minor paralysis (flattening of nasolabial folds) Partial paralysis (near or total paralysis lower face) Complete paralysis (Of upper and lower face)	0 1 2 3
5a. **Motor – Left Arm** Hold arm straight out from chest	Normal (No drift at all) Drift (Drifts downward but NOT to bed before 10 sec.) Drifts to bed within 10 sec Movement, but not against gravity Complete paralysis (No movement at all) *Amputation or joint fusion*	0 1 2 3 4 *(N/A)*
5b. **Motor – Right Arm** Hold arm straight out from chest	Normal (No drift at all) Drift (Drifts downward but NOT to bed before 10 sec.) Drifts to bed within 10 sec Movement, but not against gravity Complete paralysis (No movement at all) *Amputation or joint fusion*	0 1 2 3 4 *(N/A)*
6a. **Motor – Left leg** Keep leg off bed	Normal (No drift at all) Drift (Drifts downward but NOT to bed before 5 sec.) Drifts to bed within 5 sec Movement, but not against gravity Complete paralysis (No movement at all) *Amputation or joint fusion*	0 1 2 3 4 *(N/A)*
6b. **Motor – Right leg** Keep leg off bed	Normal (No drift at all) Drift (Drifts downward but NOT to bed before 5 sec.) Drifts to bed within 5 sec Movement, but not against gravity Complete paralysis (No movement at all) *Amputation or joint fusion*	0 1 2 3 4 *(N/A)*
7. **Limb Ataxia** Finger-Nose Heel-Knee-Shin	Absent (no ataxia, OR pt cannot move arm/leg) Present in one limb Present in two or more limbs (is absent if patient cannot understand or is too weak to do)	0 1 2
8. **Sensory** Hemisensory loss: (Test on face, arm & thigh)	Normal, no sensory loss Mild to moderate loss Severe to total sensory loss (unaware of being touched)	0 1 2
9. **Language/Aphasia** Repetition & Comprehension "Today is a bright sunny day"	Normal ability use words and follow commands Mild to Moderate (Repeats / names with some difficulty) Severe Aphasia (very few words correct or understood) Mute (no ability to speak or understand at all)	0 1 2 3
10. **Dysarthria (slurred)** Speech clarity (slurring)	Normal Mild to moderate slurred speech (some or most) Severe (unintelligible - none understandable) *Intubated or other physical barrier*	0 1 2 *(N/A)*
11. **Neglect** Ignores touch or vision to one side	No abnormality Mild (either visual or tactile – partial neglect) Profound (Visual and tactile – complete neglect)	0 1 2
Total Score	**0 = Best, 42 = Worst**	

Table 3. Modified Rankin Scale (mRS)

0: no symptoms at all
1: no significant disability despite symptoms; able to carry out all usual duties and activities
2: slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3: moderate disability; requiring some help, but able to walk without assistance
4: moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5: severe disability; bedridden, incontinent and requiring constant nursing care and attention
6: death of the patient

Table 2. Clavien-Dindo - Grading system (CDG), persistent neurological deficits and number of patients

Grade	**Definition**	**Number of patients with complications (%) at discharge (n=119)**	**Persistent new neurological deficits (“d”)**
	No complications	109 (91.6%)	
1	any deviation from normal post-operative course	2 (1.7%)	2 (100%)
2	requiring pharmacological treatment	4 (3,4%)	0 (0%)
3a	requiring surgical intervention without general anesthesia	1 (0.8%)	0 (0%)
3b	requiring surgical intervention with general anesthesia	2 (1.7%)	1 (50%)
4a	life-threatening complication, ICU, single-organ dysfunction	0 (0%)	0 (0%)
4b	life-threatening complication, ICU, multi-organ dysfunction	0 (0%)	0 (0%)
5	death of patient within 30 days	1 (0.8%)	0 (0%)

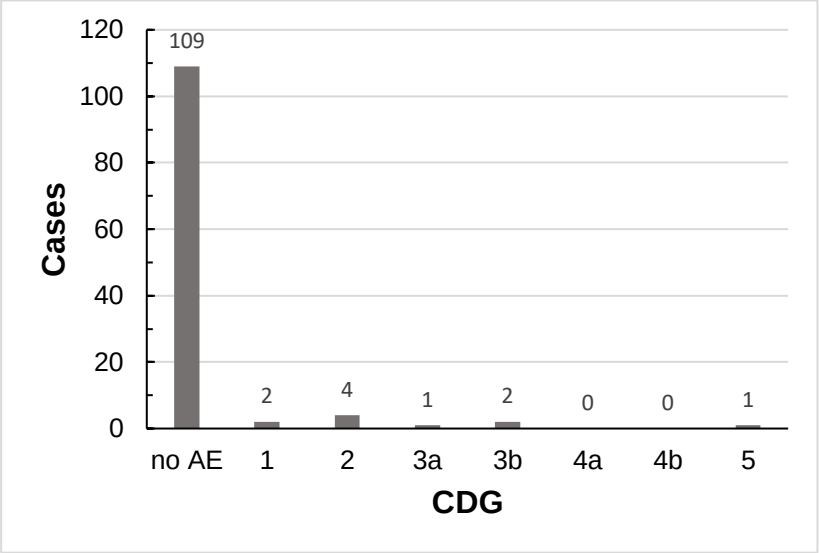

Figure 1. Distribution of patients with (CDG ≥1) and without complications at discharge (AE = adverse event)

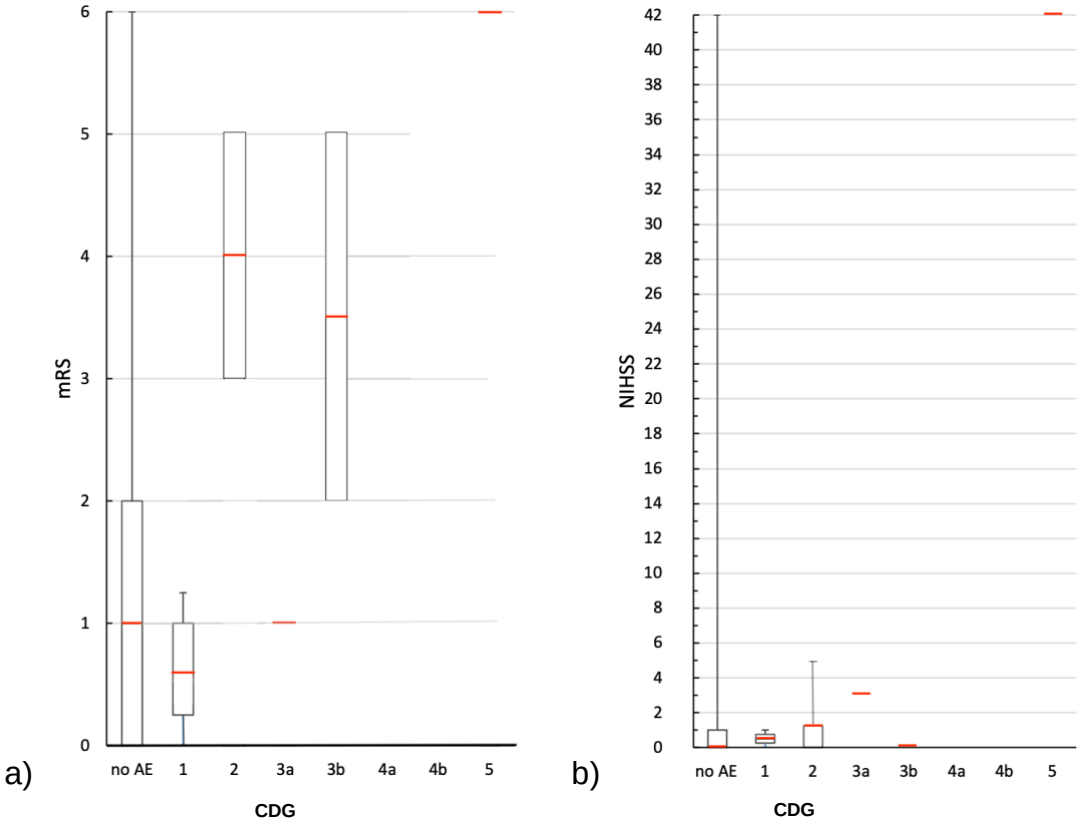

Figure 2. Correlation between complications occurring at discharge and patients' neurological performance measured with a) mRS and (b) NIHSS (AE = adverse event)

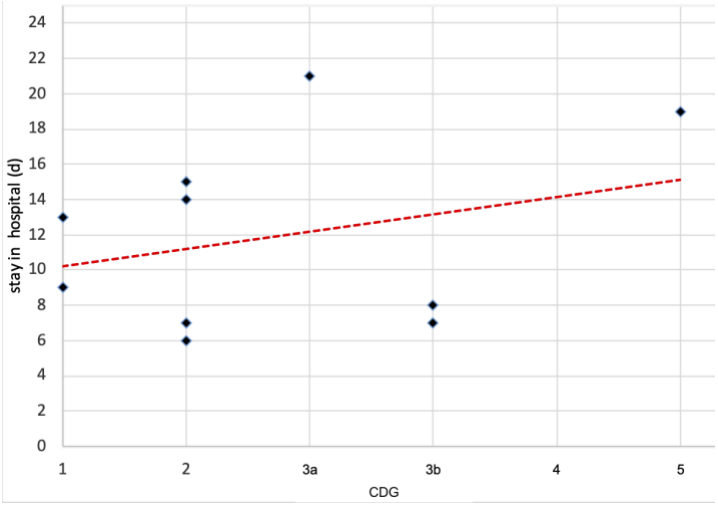

Figure 3. Correlation between complications occurring at discharge and length of hospitalization

8. Acknowledgments

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9. Lebenslauf

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10. Erklärung Masterarbeit

Ich erkläre ausdrücklich, dass es sich bei der von mir im Rahmen des Studiengangs Humanmedizin eingereichten schriftlichen Arbeit mit dem Titel:

Validation of a therapy-oriented complication grading system in carotid endarterectomy surgery

um eine von mir selbst und ohne unerlaubte Beihilfe sowie *in eigenen Worten* verfasste Masterarbeit* handelt.

Ich bestätige überdies, dass die Arbeit als Ganzes oder in Teilen weder bereits einmal zur Abgeltung anderer Studienleistungen an der Universität Zürich oder an einer anderen Universität oder Ausbildungseinrichtung eingereicht worden ist.

Verwendung von Quellen

Ich erkläre ausdrücklich, dass ich *sämtliche* in der oben genannten Arbeit enthaltenen Bezüge auf fremde Quellen (einschliesslich Tabellen, Grafiken u. Ä.) als solche kenntlich gemacht habe. Insbesondere bestätige ich, dass ich *ausnahmslos* und nach bestem Wissen sowohl bei wörtlich übernommenen Aussagen (Zitaten) als auch bei in eigenen Worten wiedergegebenen Aussagen anderer Autorinnen oder Autoren (Paraphrasen) die Urheberschaft angegeben habe.

Sanktionen

Ich nehme zur Kenntnis, dass Arbeiten, welche die Grundsätze der Selbstständigkeitserklärung verletzen – insbesondere solche, die Zitate oder Paraphrasen ohne Herkunftsangaben enthalten –, als Plagiat betrachtet werden und die entsprechenden rechtlichen und disziplinarischen Konsequenzen nach sich ziehen können (gemäss §§ 7ff der Disziplinarordnung der Universität Zürich sowie §§ 51ff der Rahmenverordnung für das Studium in den Bachelor- und Master-Studiengängen an der Medizinischen Fakultät der Universität Zürich.)

Ich bestätige mit meiner Unterschrift die Richtigkeit dieser Angaben.

Datum: 28.11.2019

Name: Muzar Vorname: Rhea Marie

Unterschrift:……..*nur auf Printversion erforderlich*

* Falls die Masterarbeit eine Publikation enthält, bei der ich Erst- oder Koautor/-in bin, wird meine eigene Arbeitsleistung im Begleittext detailliert und strukturiert beschrieben.

11. Appendix

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Chapter No.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1.
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1.
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3.1-3.2
Objectives	3	State specific objectives, including any prespecified hypotheses	3.3
Methods			
Study design	4	Present key elements of study design early in the paper	4.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4.1-4.4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4.1-4.4
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	-
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4.2-4.4
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*4.3*
Bias	9	Describe any efforts to address potential sources of bias	4.1, 4.4
Study size	10	Explain how the study size was arrived at	4.1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4.1-4.3

Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	4.4
		(*b*) Describe any methods used to examine subgroups and interactions	4.4
		(*c*) Explain how missing data were addressed	-
		(*d*) If applicable, explain how loss to follow-up was addressed	-
		(*e*) Describe any sensitivity analyses	-
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5.
		(b) Give reasons for non-participation at each stage	5.
		(c) Consider use of a flow diagram	-
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8.
		(b) Indicate number of participants with missing data for each variable of interest	-
		(c) Summarize follow-up time (e.g., average and total amount)	5.
Outcome data	15*	Report numbers of outcome events or summary measures over time	8.
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	5.
		(*b*) Report category boundaries when continuous variables were categorized	-
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses	5.
Discussion			

Key results	18	Summarize key results with reference to study objectives	6.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	6.5
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	6.
Generalisability	21	Discuss the generalisability (external validity) of the study results	6.6
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	-

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the websites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.